



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Selifonov, et al

Attorney Docket No.:  
MXGNP001X1/124.410

Application No.: 09/494,282

Examiner: Zhou, Shubo

Filed: January 18, 2000

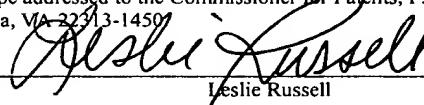
Group: 1631

Title: METHODS FOR MAKING CHARACTER  
STRINGS, POLYNUCLEOTIDES AND  
POLYPEPTIDES HAVING DESIRED  
CHARACTERISTICS

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as first-class mail on March 10, 2004 in an envelope addressed to the Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450

Signed:

  
Leslie Russell

**INFORMATION DISCLOSURE STATEMENT  
BEFORE FINAL ACTION OR NOTICE OF ALLOWANCE  
(37 CFR §§ 1.56 AND 1.97(c))**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

The references listed in the attached PTO Form 1449, a copy of which is attached, may be material to examination of the above-identified patent application. Applicants submit this reference in compliance with their duty of disclosure pursuant to 37 CFR §§1.56 and 1.97. The Examiner is requested to make this citation of official record in this application.

This Information Disclosure Statement is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that this reference indeed constitutes prior art.

This Information Disclosure Statement is being filed after the mailing date of the first Office Action on the merits, or after three months of the filing date of this application, whichever event occurred last, but it is believed before the mailing date of either: (i) a final action under §1.113 or (ii) a notice of allowance under §1.311, whichever occurs first.

Accompanying this Information Disclosure Statement is

a statement as specified in 37 CFR 1.97(e); or  
 the fee set forth in 37 CFR 1.17(p).

Enclosed is our Check No. 8773 for \$180.00 in payment of the Information Disclosure Statement Fee. If it is determined that any additional fees are due, the Commissioner is hereby authorized to charge such fees to Deposit Account 500388 (Order No. MXGNP001X1).

Respectfully submitted,  
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MAR 1 2 2004

**Form 1449 (Modified)****Information Disclosure  
Statement By Applicant**

(Use Several Sheets if Necessary)

Atty Docket No.	Application No.:
MXGNP001X1/0124.410	09/494,282
Applicant:	
Selifonov et al.	

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January 18, 2000

Group  
1631

**Other Documents**

Examiner Initial	No.	Author, Title, Date, Place (e.g. Journal) of Publication
	C1	Hellberg et al., "The Prediction of Bradykinin Potentiating Potency of Pentapeptides. An Example of a Peptide Quantitative Structure-Activity Relationship," <i>Acta Chemica Scandinavica B</i> 40, pp. 135-140, 1988
	C2	Bucht et al., "Optimising the Signal Peptide for Glycosyl Phosphatidylinositol Modification of Human Acetylcholinesterase Using Mutational Analysis and Peptide-Quantitative Structure-Activity Relationships," <i>Biochimica et Biophysica Acta</i> 1431, pp. 471-482, 1999
	C3	Sandberg et al., "Engineering Multiple Properties of a Protein by Combinatorial Mutagenesis," <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90, pp. 8367-8371, September 1993
	C4	Wrede et al., "Peptide Design Aided by Neural Networks: Biological Activity of Artificial Signal Peptidase I Cleavage Sites," <i>Biochemistry</i> , 37, pp. 3588-3593, 1998
	C5	Jill Damborsky, "Quantitative Structure-Function and Structure-Stability Relationships of Purposely Modified Proteins," <i>Protein Engineering</i> , Vol. 11, no. 1, pp. 21-30, 1998
	C6	Hellberg, et al., "Peptide Quantitative Structure-Activity Relationships, a Multivariate Approach," <i>J. Med Chem</i> , 30: pp 1126-1195, 1987
	C7	Sandberg et al., "New Chemical Descriptors Relevant for the Design of Biologically Active Peptides. A Multivariate Characterization of 87 Amino Acids," <i>J. Med Chem.</i> , 41, pp. 2481-2491, 1998
	C8	Casari et al., "A Method to Predict Functional Residues in Proteins," <i>Nat. Struct Biol.</i> , 2, pp. 171-178, 1995
	C9	Suzuki et al., "A Method for Detecting Positive Selection at Single Amino Acid Sites," <i>Mol. Biol. Evol.</i> 16 (10): pp. 1315-1328, 1999
	C10	Benner et al., "Amino Acid Substitution During Functionally Constrained Divergent Evolution of Protein Sequences," <i>Protein Engineering</i> , Vol. 7, No. 11, pp. 1323-1332, 1994



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C11	Wu et al., "Discovering Empirically Conserved Amino Acid Substitution Groups in Databases of Protein Families," Proc. Int. Conf. Intell. Syst. Mol. Biol., 4, pp. 230-240, 1996
C12	Adenot et al., "Peptides Quantitative Structure-Function Relationships: An Automated Mutation Strategy to Design Peptides and Pseudopeptides from Substitution Matrices," Journal of Molecular Graphics and Modelling, 17, pp. 292-309, 1999
C13	Norinder et al., "A Quantitative Structure-Activity Relationship Study of Some Substance P-Related Peptides," J. Peptide Res., 49, pp. 155-162, 1997
C14	Sandberg, "Deciphering Sequence Data a Multivariate Approach," Ph.D Thesis, Umea: Umea University, 78 pages, 1997
C15	Eriksson et al., "Peptide QSAR on Substance P Analogues, Enkephalins and Bradykinins Containing L-and D-Amino Acids," Acta Chemica Scandinavica, 44, pp. 50-56, 1990
C16	Ufkes et al., "Further Studies on the Structure-Activity Relationships of Bradykinin-Potentiating Peptides," European Journal of Pharmacology, 79, pp. 155-158, 1982
C17	Dobrynin et al., "Synthesis of Model Promoter for Gene Expression in Escherichia Coli," Symposium Series No. 7, pp. 365-376, 1980
C18	Skinner et al., "Potential Use of Additivity of Mutational Effects in Simplifying Protein Engineering," Proc. Natl. Acad. Sci., Vol. 93, pp. 10753-10757, 1996
C19	Lathrop et al., "Global Optimum Protein Threading with Gapped Alignment and Empirical Pair Score Functions," J. Mol. Biol., 255, pp. 641-665, 1996
C20	Hellberg et al., "A Multivariate Approach to QSAR," Ph.D. Thesis, Umea, Sweden: University of Umea: 1986
C21	Nambier et al., "Total Synthesis and Cloning of a Gene Coding for the Ribonuclease S Protein," Science, 223: 1299-1301, 1984
C22	Lin et al., "Functional Expression of Horseradish Peroxidase in E. Coli by Directed Evolution," Biotechnol. Prog, 15: 467-471, 1999
C23	Lathrop R.H., "The Protein Threading Problems with Sequence Amino Acids Interaction Preference is NP-Complete," Protein Eng., 7:1059-1068, 1994
C24	Hanes et al., "In Vitro Selection and Evolution of Functional Proteins by Using Ribosomes Display," Proc. Natl. Acad. Sci. USA, 94: 4937-4942, 1997
C25	Wells et al., "Rapid Evolution of Peptide and Protein Binding Properties <i>in vitro</i> ," Curr Opin Biotechnol, 3:355-362, 1992



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C26	Johnson et al., "The Traveling Salesman Problem: A Case Study in Local Optimization," In Local Search in Combinatorial Optimization, Edited by Aarts et al., John Wiley & Sons Ltd., 21-310, 1997
C28	Jonsson et al., "Quantitative Sequence-Activity Models (QSAM) – Tools for Sequence Design," Nucleic Acids Res., 21:733-739, 1993
C29	Geladi et al., "Partial Least Squares Regression: A Tutorial," Anal Chim Acta, 168: 1-17, 1986
C30	Holowachuk et al., "Efficient Gene Synthesis by Klenow Assembly/Extension-Pfu Polymerase Amplification (KAPPA) of Overlapping Oligonucleotides," PCR Methods Appl, 4:299-302, 1995
C31	Hellberg et al., "Minimum Analogue Peptide Sets (MAPS) for Quantitative Structure-Activity Relationships," Int J Pept Protein Res, 37:414-424, 1991
C32	Mee et al., "Design of Active Analogues of a 15-Residue Peptide Using D-Optimal Design, QSAR and a Combinatorial Search Algorithm," J Pept Res, 49:89-102, 1997
C33	Schneider et al., "Peptide Design by Artificial Neural Networks and Computer-Based Evolutionary Search," Proc Natl Acad Sci USA, 95:12179-12184, 1998
C34	Sjostrom et al., "Signal Peptide Amino Acid Sequences in Escharichla Coli Contain Information Related to Final Protein Localization, A Multivariate Data Analysis," EMBO, 6:823-891, 1987
C35	Patel et al., "Patenting Computer-Designed Peptides," Journal of Computer-Aided Molecular Design, 12:543-556, 1998
C36	Aita et al., "Theory of Evolutionary Molecular Engineering Through Simultaneous Accumulation of Advantageous Mutations," J. Theor. Biol., 207:543-556, 2000
C37	Darius et al., "Simulated Molecular Evolution of Computer Generated Artifacts?," Biophysical Journal, 67:2120-2122, 1994
C38	Singh et al., "Application of Genetic Algorithms to Combinatorial Synthesis: A Computational Approach to Lead Identification and Lead Optimization," J.Am. Chem. Soc., 118:1669-1676, 1996
	Date Considered

Examiner: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.